REMARKS/ARGUMENTS

The Office Action mailed October 4, 2005 has been carefully reviewed. Reconsideration of this application, as amended and in view of the following remarks, is respectfully requested. The claims presented for examination are: claims 1-19.

35 USC 112 REJECTION

In numbered paragraph 3 of the Office Action mailed October 4, 2005, claims 1-5 and 16-19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It was pointed out that the preamble "consisting of" is used yet the claims only describe "chambers" and do not include sufficient elements. It was requested that "the claims recite specific structural elements that define a device that capable of functioning as recite in the preamble of the claim."

Applicants have amended the claims so that the preamble states: "A microfabricated biopsy and analysis instrument for biopsy and analysis of tissue with minimal handling of the tissue, consisting of:" Applicants have also amended the claims so that the claims recite specific structural elements that define a device that capable of functioning as recite in the preamble.

Applicants believe that the amended claims now comply with the requirement of 35 U.S.C. 112, second paragraph, and that Applicants have provided a full and complete response to the 35 U.S.C. 112, second paragraph, rejection in numbered paragraph 3 of the Office Action mailed October 4, 2005.

35 USC 103 Rejection

In numbered paragraph 7 of the Office Action mailed October 4, 2005 claims 1-5 and 16-19 were rejected under 35 U.S.C. 103(a) as being allegedly

unpatentable over the primary Pourahmadi et al reference (International Patent No. WO 99/33559) in view of the secondary Krulevitch et al references (U.S. Patent No. 5,985,217 or U.S. Patent No. 6,319,474).

Applicants have amended claims 1-5 and 16-19; therefore all the claims presented for examination are now in amended form. Since amended claims 1-5 and 16-19 now presented for examination appear in amended form, the 35 USC §103(a) rejection in the Office Action mailed October 4, 2005 no longer applies.

Applicants believe that amended claims 1-5 and 16-19 now presented for examination are patentable and that the Pourahmadi et al and Krulevitch et al references would not support a 35 USC §103(a) rejection. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) include "Ascertaining the differences between the prior art and the claims at issue."

The differences between the primary Pourahmadi et al reference and Applicants' invention defined by amended claims 1-5 and 16-19 is that the microfabricated biopsy and analysis instrument for biopsy and analysis of tissue with minimal handling of the tissue consisting of the combination of elements of amended claims 1-5 and 16-19 is not found in the primary Pourahmadi et al reference.

For example claim 1 specifies "a microfabricated biopsy and analysis instrument for biopsy and analysis of tissue with minimal handling of the tissue, consisting of:

a body comprising a silicon substrate and a glass substrate positioned together,

a cutter having a tapered opening with a sharp edge for cutting the tissue, said cutter located in said silicon substrate, a specimen chamber located in said silicon substrate and said glass substrate immediately below said cutter, said specimen chamber positioned to directly receive the tissue cut by said cutter,

a specimen treatment and analysis chamber located in said silicon substrate and said glass substrate abutting and connected directly to said specimen chamber and located adjacent said specimen chamber,

an analysis unit in said specimen treatment and analysis chamber,

a PCR reaction chamber located in said silicon substrate and said glass substrate directly abutting and connected directly to said specimen treatment and analysis chamber, said PCR reaction chamber constructed to receive the tissue from said specimen treatment and analysis chamber, and

a heating unit in said body adjacent said PCR reaction chamber."

The Pourahmadi et al reference includes a much different combination of elements. The Pourahmadi et al device is described in the Pourahmadi et al reference beginning at page 10, line 17 and continuing through page 13, line 2 and in FIG. 2 set out below:

The Pourahmadi et al Reference

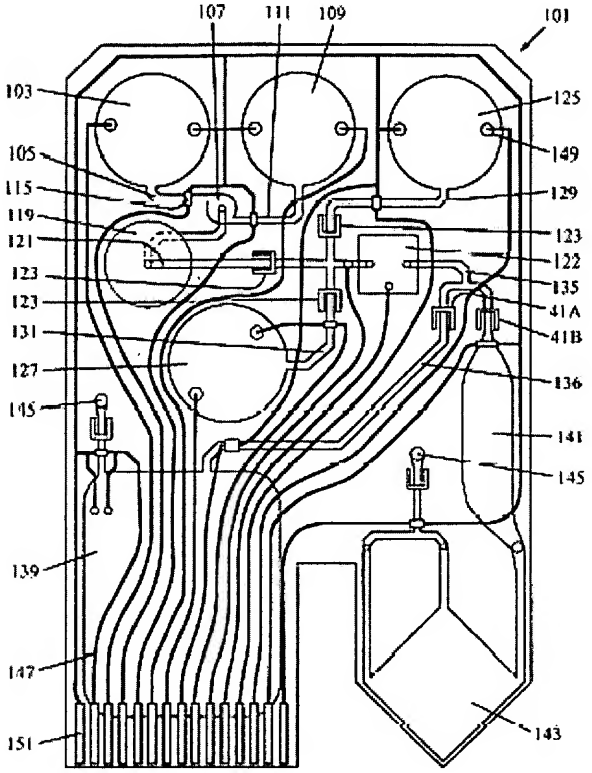

FIG. 2

"Fig. 2 shows an example of a cartridge 101 according to a preferred embodiment of the invention. The cartridge is designed to process a fluid sample and amplify nucleic acids, such as by polymerase chain reaction (PCR). The cartridge 101 includes a sample port 103 for introducing a fluid sample into the cartridge and a sample flow path extending from the port 103 into the body of the cartridge.

The sample flow path includes a channel 105 leading from the sample part 103 to a mixing chamber 107 for mixing of the sample with lysing reagents. The sample flow path also includes a lysing chamber 119 where the sample contacts a filter to capture components, e.g., cells, spores, or microorganisms in the sample. The captured components are lysed in chamber 119. The sample flow path further includes a flow-through component 122 for capturing a desired analyte, e.g., nucleic acid, from the sample as the sample flows through the component 122.

The flow-through component 122 is preferably a microfabricated chip having a chamber with internal microstructures formed therein. The microstructures have sufficiently high surface area and binding affinity with the desired analyte to capture the analyte as the sample flows

through the chip. The microstructures preferably comprise an array of columns integrally formed with at least one wall of the chamber and extending into the chamber. Various embodiments of the microfabricated chip are described in detail below with reference to Figs. 6-14.

In an alternative embodiment, the flow-through component 122 comprises a channel or chamber formed in the cartridge. The channel or chamber contains at least one solid support for capturing the desired analyte from the fluid sample as the sample flows through the solid support. Suitable solid supports include filters, beads, fibers, membranes, glass wool, filter paper, polymers and gels.

The sample flow path also includes a channel 135 leading to flow controllers 41A and 41B, and a channel 136 leading to a vented waste chamber 139. The flow controllers 41A and 41B are arranged to direct the sample into the waste chamber 139 after the sample flows through the capture component 122.

The flow controllers 41A and 41B may be, e.g., valves, flow diverters, or fluid diodes.

A flow path for carrying elution fluid is also formed in the cartridge 101. In the preferred embodiment, the cartridge includes a storage chamber 127 for storing elution fluid.

The elution flow path extends from the chamber 127 through a channel 131 and passes through the flowthrough component 122, thereby releasing captured analyte from the component into the elution fluid. In an alternative embodiment, the cartridge includes a separate inlet port, in place of or in addition to the storage chamber 127, for introducing elution fluid into the cartridge from an external source.

The elution flow path diverges from the sample flow path after passing through the component 122. In this example, the elution flow path follows the channel 135 to the flow controllers 41A and 41B. The flow controllers 41A and 41B are arranged to direct the elution fluid and eluted analyte into a reagent chamber 141 containing PCR reagents. The reagent chamber 141 is in fluid communication with a reaction chamber 143 for PCR amplification.

The reaction chamber 143 may be a chamber formed in the cartridge 101. Alternatively, the reaction chamber 143 may be formed in a separate reaction vessel designed to be coupled to the cartridge to receive the eluted analyte.

> Suitable reaction vessels for this purpose are disclosed in International Application Number PCT/US98/03962 filed March 2, 1998 and entitled "Heat Exchanging, Optically Interrogated Chemical Reaction Assembly", the disclosure of which is incorporated by reference herein. The application also teaches a thermal sleeve for receiving and thermally cycling the reaction chamber. For this reason, it is advantageous for the reaction chamber to protrude from the rest of the cartridge body to facilitate insertion of the reaction chamber into the thermal sleeve.
>
> The cartridge 101 also includes a storage chamber 109 for storing a lysing reagent, and a storage chamber 125 for storing a washing reagent. The cartridge 101 further includes flow controllers 123, such as valves or fluid diodes, for controlling the flow of fluid through the cartridge. The cartridge 101 also preferably includes resistive sensors 115 for sensing the presence of fluid in various channels and regions."

Applicants' invention defined by amended claims 1- 5 and 16-19 provides the specific combination of elements that produces a microfabricated biopsy and analysis instrument that is compact, efficient, simple to operate. Applicants' invention defined by amended claims 1- 5 and 16-19 is very different from the highly complex system disclosed in the Pourahmadi et al reference. Since the combination of elements of Applicants' amended claims 1- 5 and 16-19 is not found in the Pourahmadi et al reference, the Pourahmadi et al reference would not support a 35 USC §102(b) rejection of amended claims 1- 5 and 16-19.

The Krulevitch et al references also fail to show the elements and combination of elements of amended claims 1- 5 and 16-19. Since the Pourahmadi et al reference and the Krulevitch et al references fail to show the elements and combination of elements, there can be no combination of the references that would show Applicant's invention defined by amended claims 1- 5 and 16-19 now presented for examination and render them unpatentable.

There is no combination of the Pourahmadi et al reference and the Krulevitch et al references that would produce the combination of elements of

Applicants' amended claims 1- 5 and 16-19. Further, there is no teaching of combining the Pourahmadi et al reference and the Krulevitch et al references to meet Applicants' amended claims 1- 5 and 16-19 now presented for examination.

Under MPEP §2142, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. It should be noted that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Since there is no suggestion or motivation to combine the references to produce Applicant's invention, a 35 U.S.C. §103(a) rejection of Applicant's claims would not be appropriate.

Obviousness-Type Double Patenting Rejection - U.S. Patent No. 5,985,217

In numbered paragraph 8 of the Office Action mailed October 4, 2005 claims 1-5 and 16-19 were rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-15 of the Krulevitch et al reference (U.S. Patent No. 5,985,217) in view of the Pourahmadi et al reference (International Patent No. WO 99/33559).

It was stated, "A timely filed terminal disclaimer in compliance with 37CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatuatory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application."

The Krulevitch et al reference (U.S. Patent No. 5,985,217) and the subject application are commonly owned. Both the Krulevitch et al reference (U.S. Patent No. 5,985,217) and the subject application are owned by The Regents of the University of California. The Krulevitch et al reference (U.S. Patent No. 5,985,217) on its face shows that it is owned by The Regents of the University of California.

The subject application is also owned by The Regents of the University of California as shown by an assignment recorded in the United States Patent and Trademark Office.

Enclosed herewith is a terminal disclaimer in compliance with 37 CFR 1.321(c), disclaiming the terminal portion of any patent issue from this application which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. 154 to 156 and 173 of prior U.S. Patent No. 5,985,217.

Applicants believe they have provided a full and complete response to the obviousness-type double patenting rejections in numbered paragraph 8 of the Office Action mailed October 4, 2005.

Obviousness-Type Double Patenting Rejection - U.S. Patent No. 6,319,474

In numbered paragraph 9 of the Office Action mailed October 4, 2005 claims 1-5 and 16-19 were rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-15 of the Krulevitch et al reference (U.S. Patent No. 6,319,474) in view of the Pourahmadi et al reference (International Patent No. WO 99/33559).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatuatory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. Enclosed herewith is a terminal disclaimer in compliance with 37 CFR 1.321(c), disclaiming the terminal portion of any patent issue from this application which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. 154 to 156 and 173 of prior U.S. Patent No. 6,319,474.

The Krulevitch et al reference (U.S. Patent No. 6,319,474) and the subject application are commonly owned. Both the Krulevitch et al reference (U.S. Patent No. 6,319,474) and the subject application are owned by The Regents of the

University of California. The Krulevitch et al reference (U.S. Patent No. 6,319,474) on its face shows that it is owned by The Regents of the University of California. The subject application is also owned by The Regents of the University of California as shown by an assignment recorded in the United States Patent and Trademark Office.

Applicants believe they have provided a full and complete response to the obviousness-type double patenting rejections in numbered paragraph 9 of the Office Action mailed October 4, 2005.

SUMMARY

The undersigned respectfully submits that, in view of the foregoing amendments and the foregoing remarks, the rejections of the claims raised in the Office Action dated October 4, 2005 have been fully addressed and overcome, and the present application is believed to be in condition for allowance. It is respectfully requested that this application be reconsidered, that the claims be allowed, and that this case be passed to issue. If it is believed that a telephone conversation would expedite the prosecution of the present application, or clarify matters with regard to its allowance, the Examiner is invited to call the undersigned attorney at (925) 424-6897.

Respectfully submitted,

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Livermore, California
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